

# **Drug Therapy of Peptic Ulcer & Gastroesophageal Reflux Disease (GERD)**

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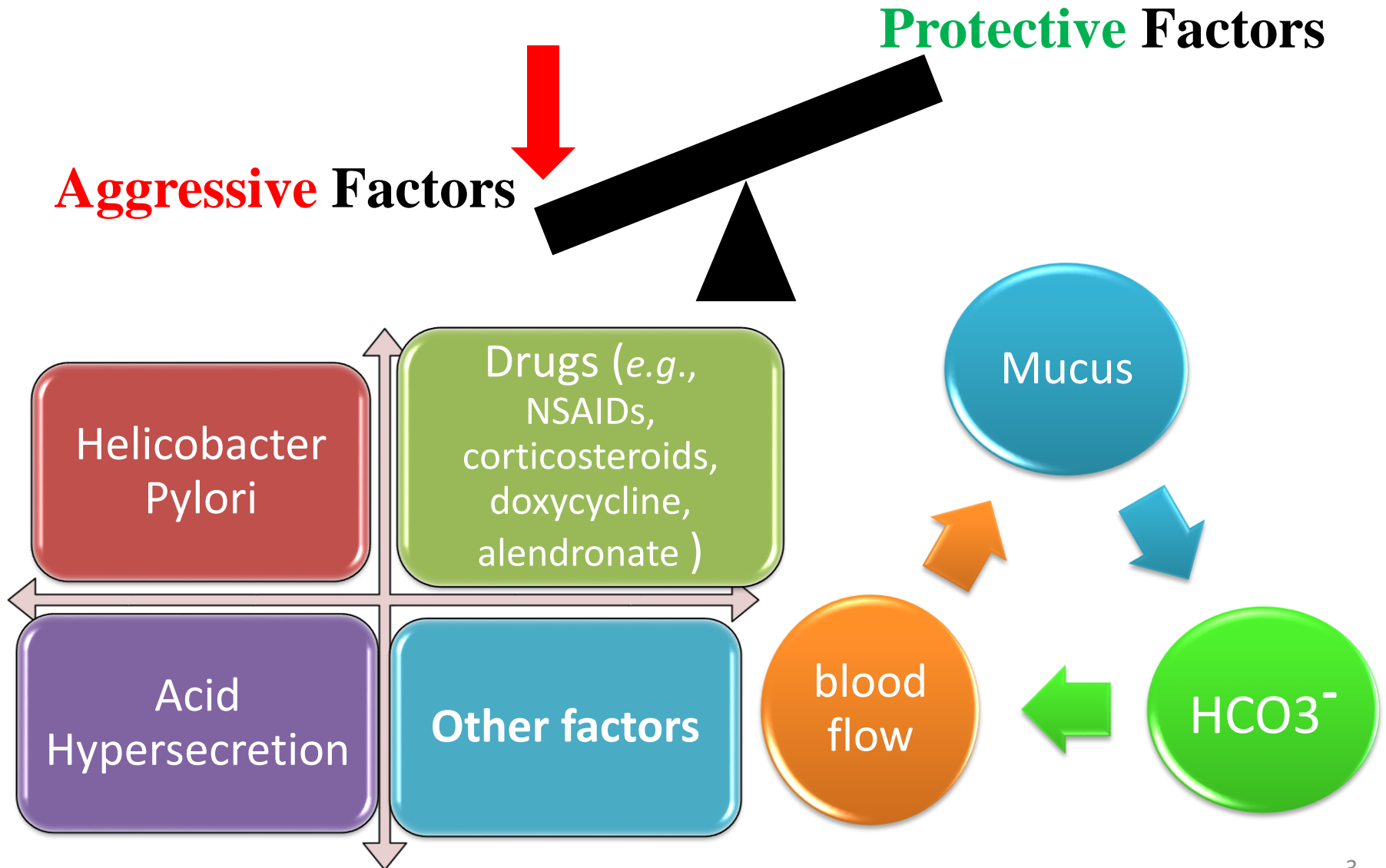
Tanta University

## Peptic ulcer

A break in the mucosa of the stomach (*gastric ulcer*) or duodenum (*duodenal ulcer*)

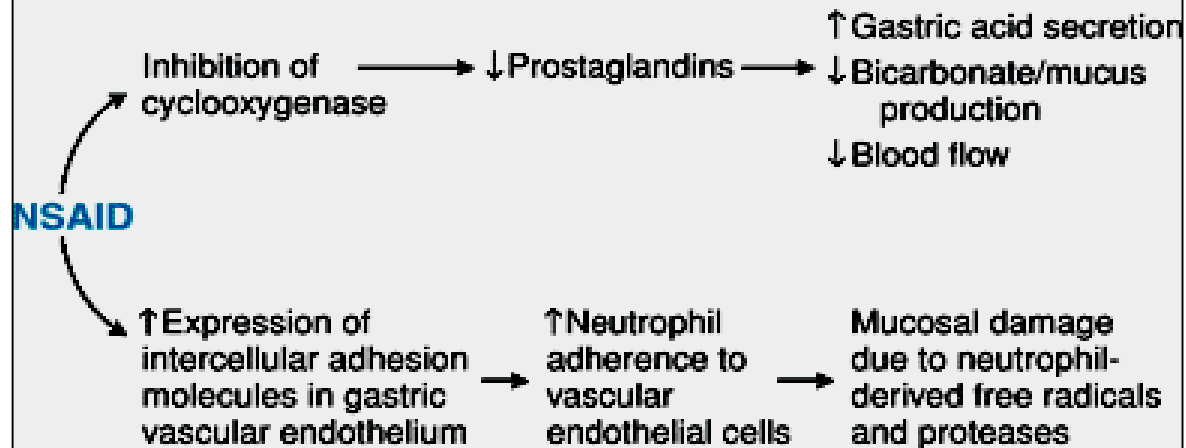
**Symptoms:** Burning pain → bleeding → obstruction or perforation.

# Pathophysiology of Peptic Ulcer Disease



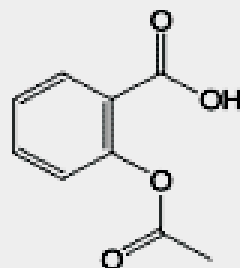
# NSAID-induced Peptic Ulcer

## A Systemic effects



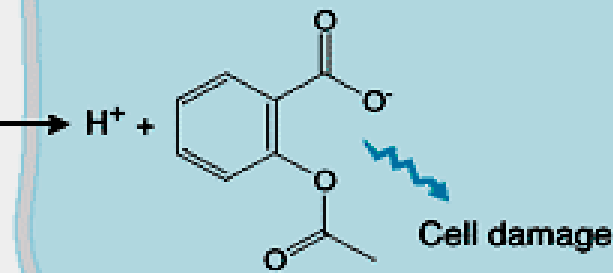
## B Topical injury

Stomach lumen  
(pH  $\approx$  2)

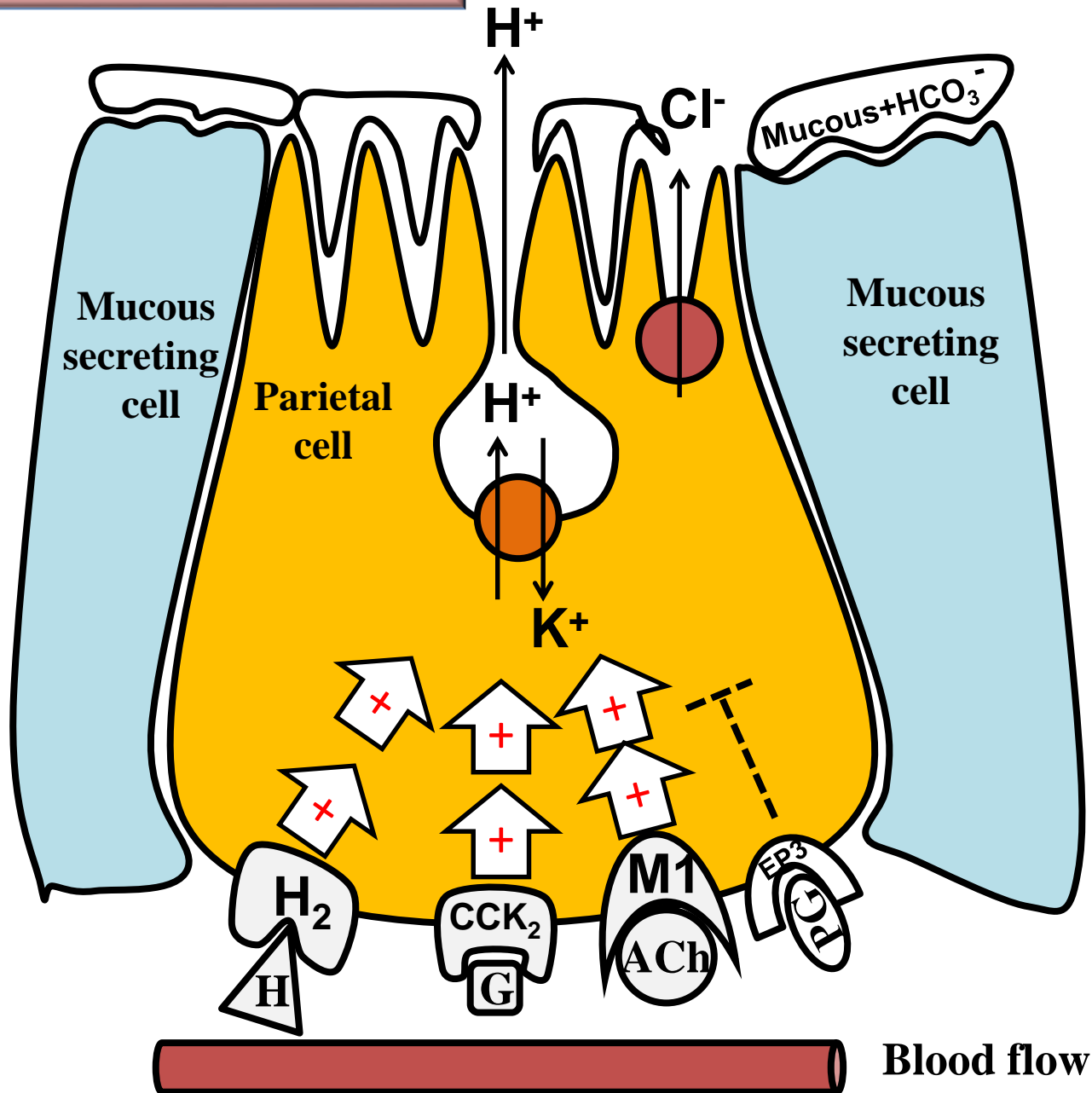


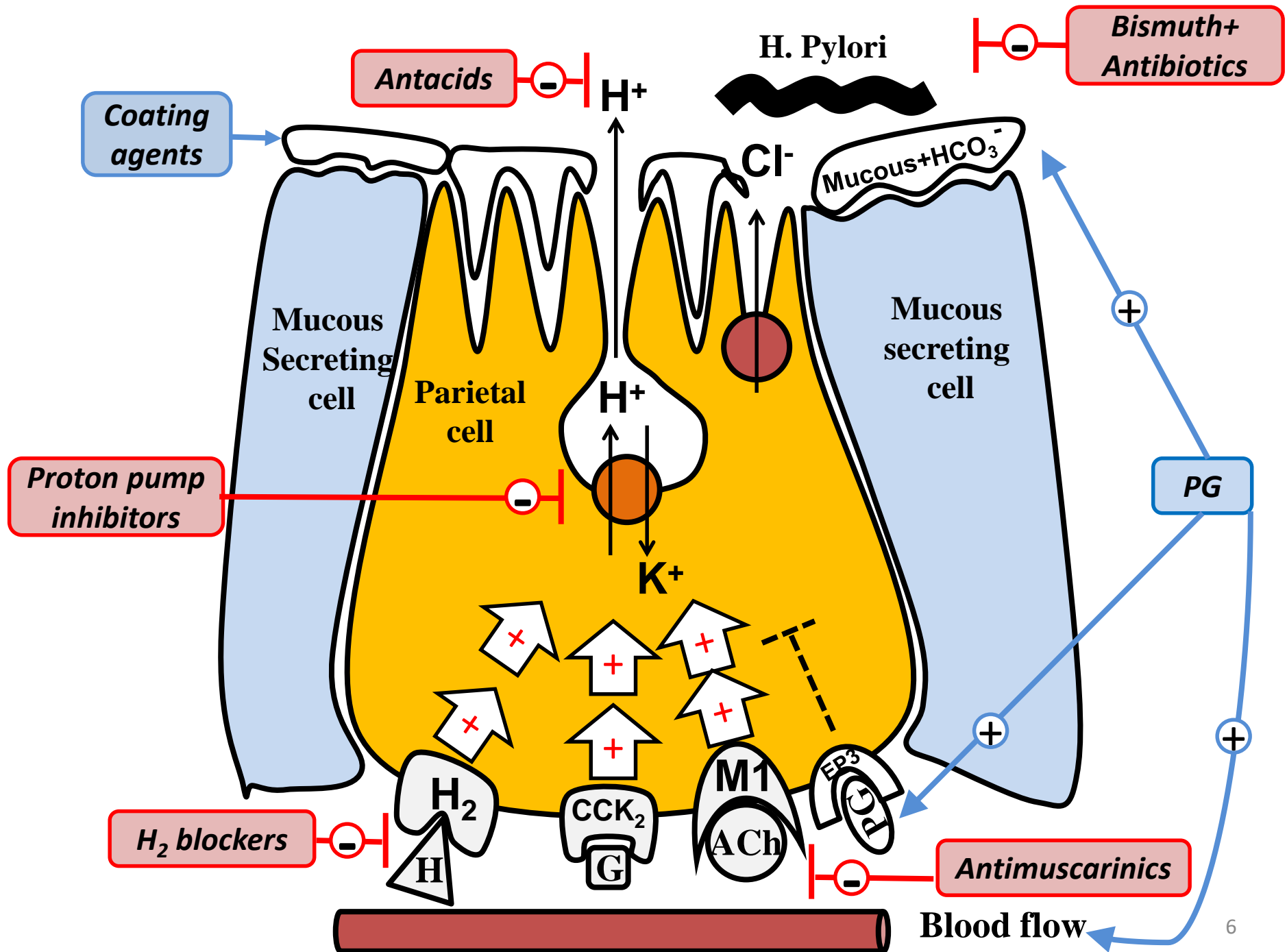
NSAID (aspirin)  
weak acid

Gastric epithelial cell  
(pH  $\approx$  7)

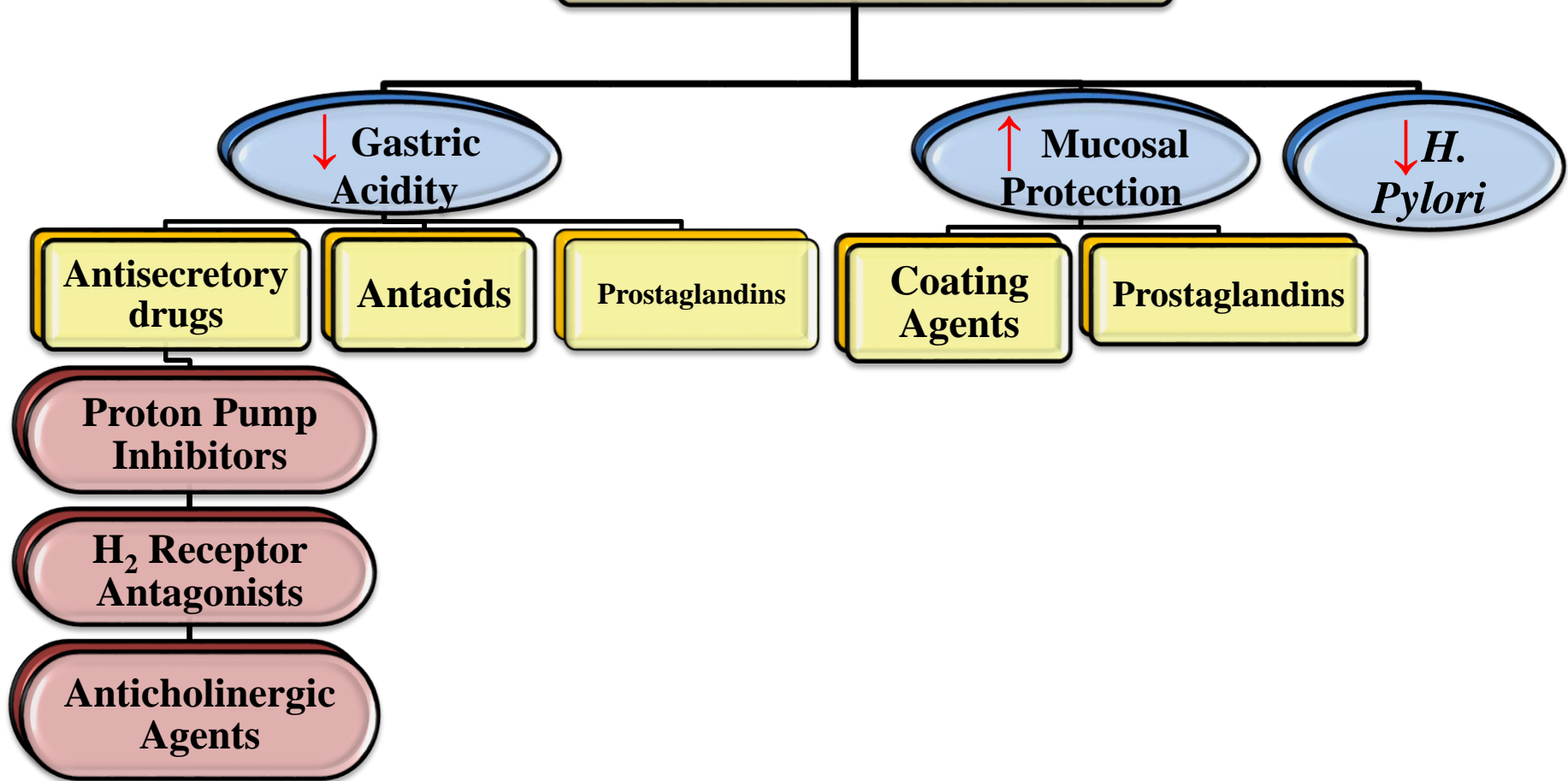


# Gastric acid secretion

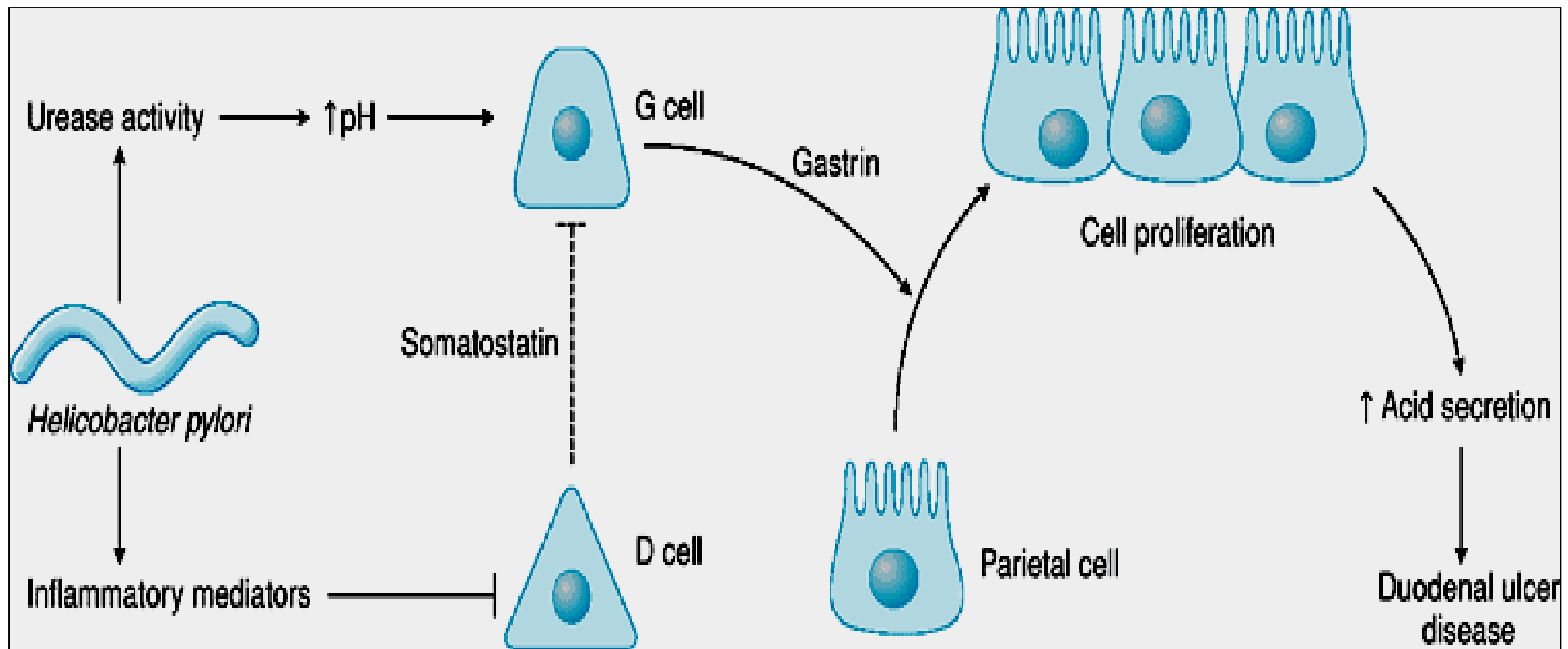




# Treatment Strategy of Peptic Ulcer



↓ gastric acidity → ↓ absorption of some drugs e.g., Itraconazole and digoxin.



## *H. Pylori*-induced Peptic Ulcer



# Treatment of H. Pylori

## Triple therapy

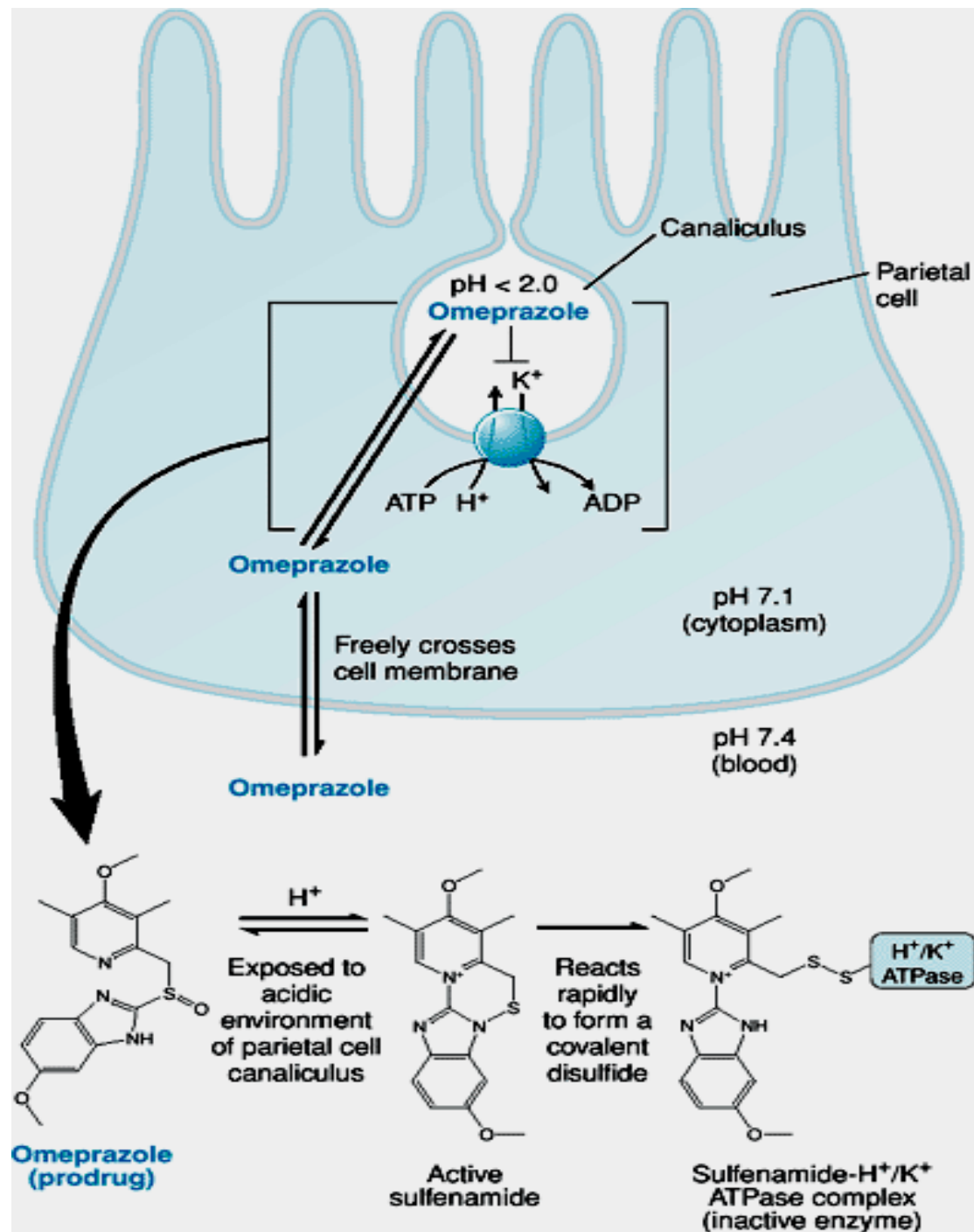
Amoxicillin + clarithromycin + a proton pump inhibitor.

Tinidazole + clarithromycin + a proton pump inhibitor

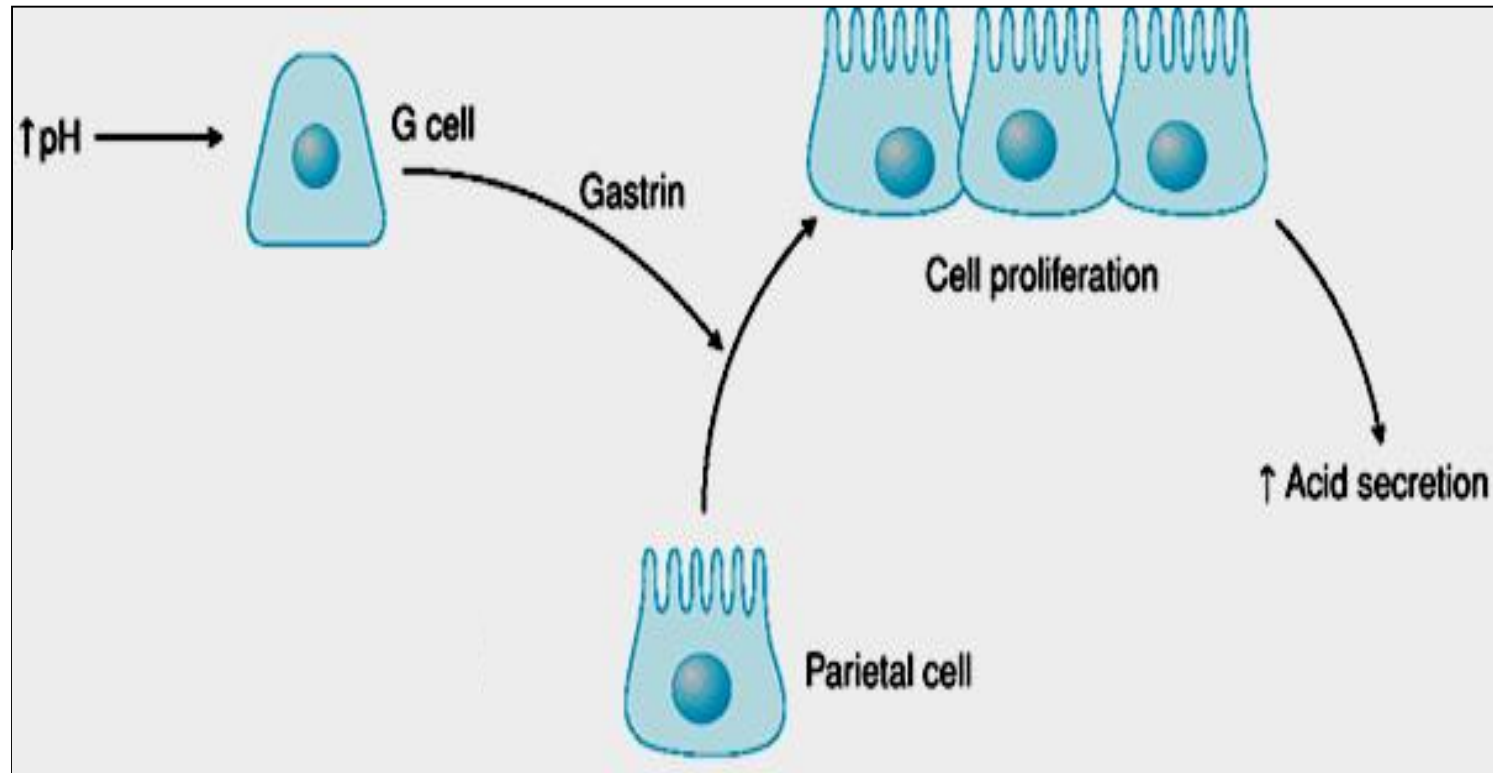
## Quadruple therapy

Tetracycline+ metronidazole + bismuth + a proton pump inhibitor  
(or H<sub>2</sub> antagonist).

***\*\*\*Resistance of H. pylori to metronidazole and clarithromycin has been reported.***



**PPI use  $\rightarrow$   $\uparrow$ plasma gastrin $\rightarrow$  hyperplasia of parietal cells $\rightarrow$  rebound  $\uparrow$ acid secretion upon discontinuation**





**Proton Pump Inhibitors**  
*e.g., Omeprazole, esomeprazole,  
 rabeprazole, lansoprazole,  
 pantoprazole*

**H<sub>2</sub> Receptor Antagonists**  
*e.g., cimetidine, ranitidine,  
 famotidine, and nizatidine*

**Anticholin-  
 ergic Agents**  
*e.g., Pirenzepine*

**M.O.A**

prodrugs → *sulfenamide* (active)  
 → binds (irrevers.) cysteine  
 residue on H<sup>+</sup>/K<sup>+</sup>-ATPase →  
 gastric pH > 6

Block H<sub>2</sub> receptors  
 reversibly and  
 competitively

Block M<sub>1</sub>  
 receptors (low  
 efficacy)

**PK**

- Enteric coating (??)
- Metabolized by CYP450,  
 except rabeprazole (non-  
 enzymatic pathway)

- ⊖ CYP450 (*Cimetidine*)
- hepatic & renal  
 elimination, except  
 nizatidine (only renal).

**S.E.**

Rebound acid hypersecretion  
 (due to hypergastrinemia →  
 hyperplasia of ECL & parietal  
 cells).  
 VitB12 & calcium deficiencies,  
 Gastroenteritis

Gynecomastia  
 & galactorrhea  
 (*Cimetidine*,  
 antiandrogenic effects)

Atropine-like  
 side effects

**Antisecretory  
drugs**

## **Prostaglandins**

e.g., Misoprostol

<b>M.O.A</b>	a PGE1 analogue: 1) ↓ gastric acid secretion 2) ↑ bicarbonate & mucus secretion 3) ↑ blood flow
<b>PK</b>	<ul style="list-style-type: none"><li>▪ Taken with meals</li><li>▪ Short <math>t_{1/2}</math> (4 times daily)</li></ul>
<b>S.E.</b>	<ul style="list-style-type: none"><li>➤ Abdominal cramps and diarrhea</li><li>➤ ↑ uterine contractions (Abortion, uterine rupture)</li></ul>

# Antacids

*e.g., Mixture of aluminum hydroxide & magnesium hydroxide,  
sodium bicarbonate, calcium carbonate*

## *Mechanism of action:*

Neutralization of gastric acid.

## *Contraindications:*

- Hypertension .
- Chronic kidney disease.

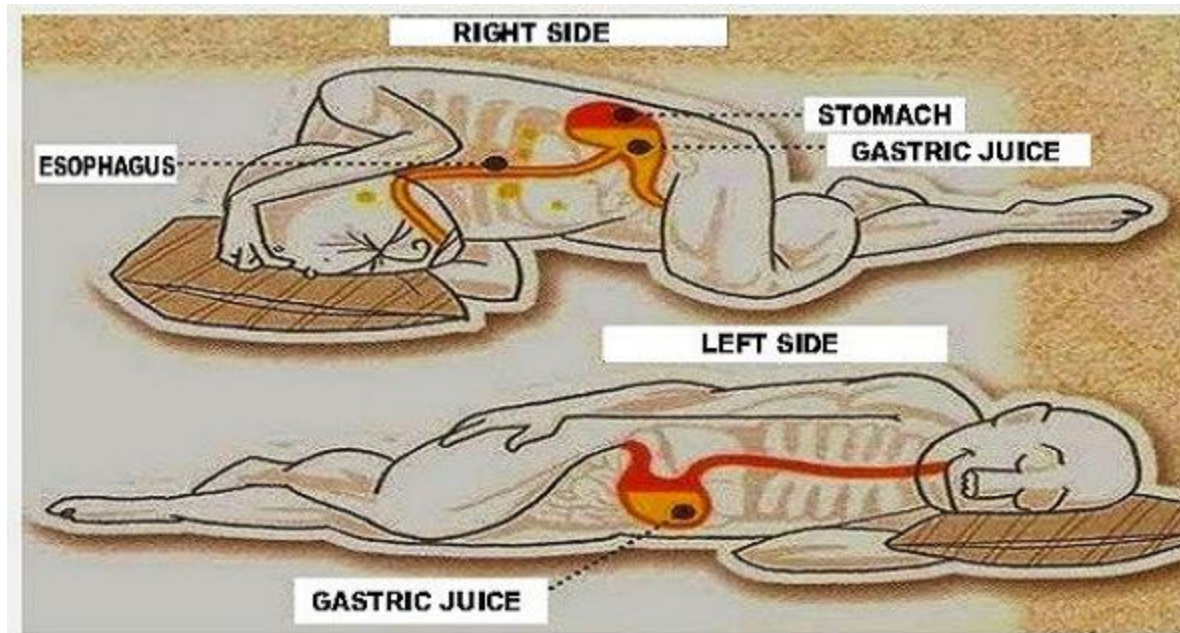
## ↑ Mucosal Protection

	Coating agents		Prostaglandins e.g., Misoprostol
	Sucralfate	Colloidal bismuth	
<b>M.O.A</b>	Viscous gel (gastric acidity)→ adheres to positively charged proteins in ulcerated areas	<ul style="list-style-type: none"> <li>▪ Bismuth salts combine with mucus glycoproteins</li> <li>▪ ↑ bicarbonate and PGE<sub>2</sub> secretion</li> </ul>	a PGE <sub>1</sub> analogue: <ol style="list-style-type: none"> <li>1) ↓ gastric acid secretion</li> <li>2) ↑ bicarbonate &amp; mucus secretion</li> <li>3) ↑ blood flow</li> </ol>
<b>PK</b>	Non absorbable (poorly soluble complex salt of sucrose sulfate and aluminum hydroxide)		<ul style="list-style-type: none"> <li>▪ Taken with meals</li> <li>▪ Short t<sub>1/2</sub> (4 times daily)</li> </ul>
<b>S.E.</b>	No systemic toxicity		<ul style="list-style-type: none"> <li>➤ Abdominal cramps and diarrhea</li> <li>➤ ↑ uterine contractions (Abortion, uterine rupture)</li> </ul>

# Gastroesophageal Reflux Disease (GERD)

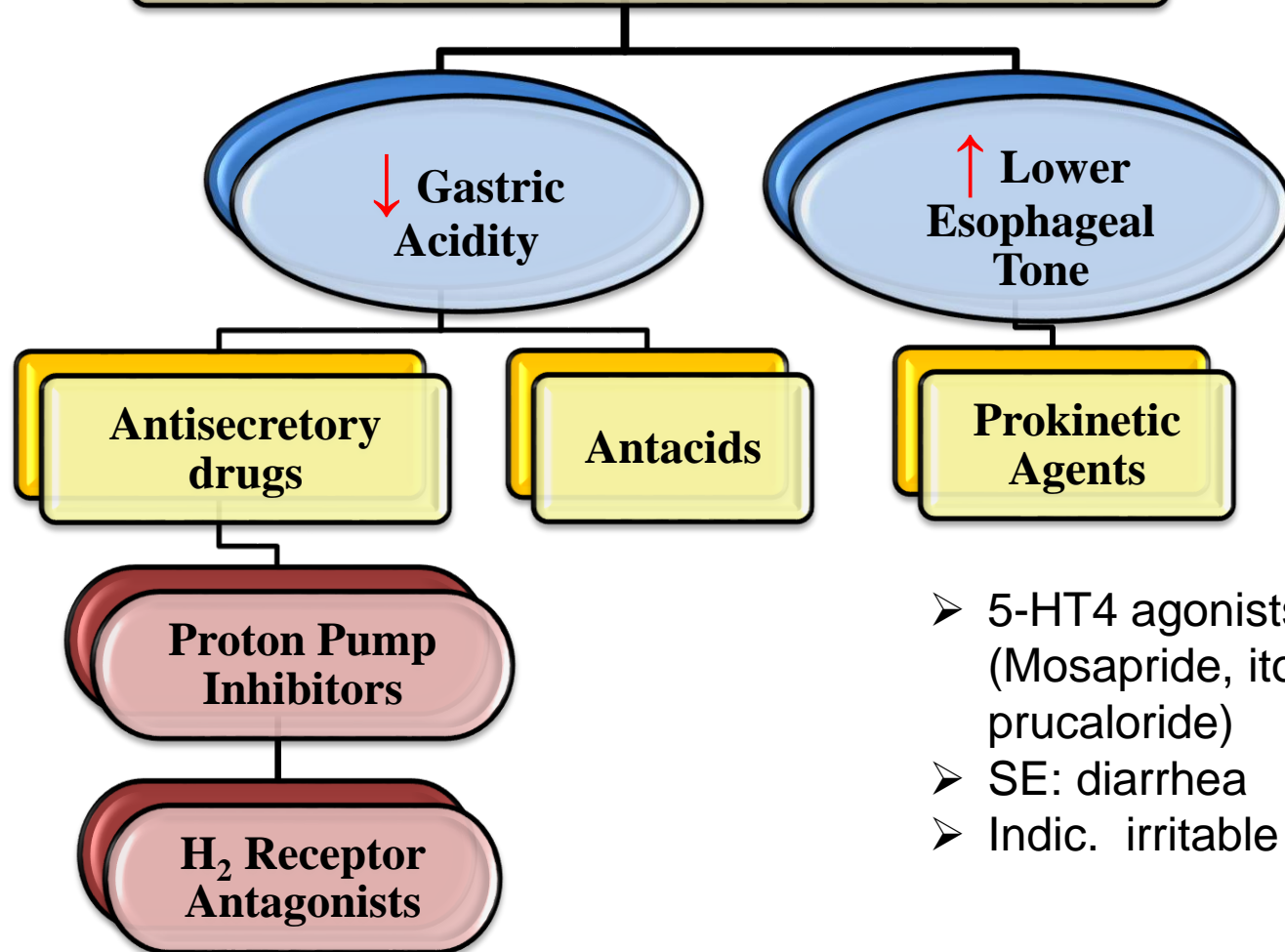
Gastroesophageal regurgitation → →injurious effects of the refluxed gastric content on the esophageal epithelium

**Symptoms:** Heartburn, chest Pain, cough, asthma, sore throat, hoarseness of voice & dental carries





# Treatment strategy of GERD



- 5-HT<sub>4</sub> agonists (Mosapride, itopride, prucaloride)
- SE: diarrhea
- Indic. irritable colon).